Bone Resorption Is Affected by Follicular Phase Length in Female Rotating Shift Workers

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Stressors as subtle as night work or shift work can lead to irregular menstrual cycles, and changes in reproductive hormone profiles can adversely affect bone health. This study was conducted to determine if stresses associated with the disruption of regular work schedule can induce alterations in ovarian function which, in turn, are associated with transient bone resorption. Urine samples from 12 rotating shift workers from a textile mill in Anqing, China, were collected in 1996–1998 during pairs of sequential menstrual cycles, of which one was longer than the other (28.4 vs. 37.4 days). Longer cycles were characterized by a prolonged follicular phase. Work schedules during the luteal-follicular phase transition (LFPT) preceding each of the two cycles were evaluated. All but one of the shorter cycles were associated with regular, forward phase work shift progression during the preceding LFPT. In contrast, five longer cycles were preceded by a work shift interrupted either by an irregular shift or a number of "off days." Urinary follicle-stimulating hormone levels were reduced in the LFPT preceding longer cycles compared with those in the LFPT preceding shorter cycles. There was greater bone resorption in the follicular phase of longer cycles than in that of shorter cycles, as measured by urinary deoxypyridinoline. These data confirm reports that changes in work shift can lead to irregularity in menstrual cycle length. In addition, these data indicate that there may be an association between accelerated bone resorption in menstrual cycles and changes of regularity in work schedule during the preceding LFPT. *Key words:* bone resorption, deoxypyridinoline (DPD), follicular phase length, luteal-follicular phase transition (LFPT), shift work. *Environ Health Perspect* 111:618–622 (2003). doi:10.1289/ehp.5878 available via *http://dx.doi.org/* [Online 9 December 2002]

Although the association between ovarian function and bone loss is well recognized, the minimal hormonal requirements for maintaining healthy bones are poorly defined. Exercise-induced amenorrhea (Beitins et al. 1991; Broocks et al. 1990; Bullen et al. 1985), prolactin-secreting tumors (Klibanski et al. 1980; Schlechte et al. 1983), and gonadotropin-releasing hormone (GnRH)-induced hypogonadism (Scharla et al. 1990; Surrey and Judd 1992) all result in bone loss in women. Female athletes have been shown to lose bone despite increased skeletal loading, a situation that places these women at increased risk for bone injuries (Cann et al. 1984). Older studies suggested that bone loss in healthy young women is related to abnormalities of progesterone production (Bullen et al. 1985; Prior 1990). However, recent reports have indicated that even modest exercise can result in alterations of ovarian function characterized by perturbations of the follicular phase but not the luteal phase of the menstrual cycle (De Souza et al. 1997; Waller et al. 1996; Winters et al. 1996). These subtle alterations of the follicular phase were associated with decreased bone integrity and an increased incidence of bone fractures (De Souza et al. 1997). Other data suggest that stress-related effects on bone health are associated with alterations in the rise of follicle-stimulating hormone (FSH) during the late luteal phase of the menstrual cycle, which in turn alter the follicular phase of the next cycle (De Souza et al. 1998).

The number of women in the workforce has grown over the past 20 years and continues to expand. Because a majority of working women are in their reproductive years, there is public concern about exposures in the workplace that could adversely affect menstrual function, fertility, or pregnancy. As a consequence of this concern, several studies have been designed to identify such hazards (Eskenazi et al. 1995; Gold et al. 1995a, 1995b; Lasley et al. 1995; Schenker et al. 1995). Despite clear evidence that subtle stressors such as changes in work schedule also may have adverse effects on reproductive health, there have been few studies on such nonchemical hazards, and there is little understanding of their mechanism(s) of action. Such stressors not only may have intrinsic adverse effects, but also they may exacerbate the effects of other workplace hazards. The presence of these stressors also can confound interpretation of the results of studies designed to evaluate other putative hazards.

Previous studies have indicated that stressors as subtle as night work or shift work can lead to irregular menstrual cycles (Miyauchi et al. 1992) through perturbations of the diurnal rhythms of reproductive hormones. The present study was conducted to test the hypothesis that stresses associated with the disruption of the regular work schedule induce alterations in ovarian function which, in turn, are associated with transient bone resorption. Specifically, we assessed work shift status, ovarian hormone profiles, and bone metabolites during two consecutive menstrual cycles of female workers to determine if a delay of ovulation and lengthening of the follicular phase are induced by the changing of work-shift regularity, and if these alterations of the menstrual cycle are associated with increased bone resorption.

Materials and Methods

Subjects. Twenty-one healthy Chinese female workers on rotating work shifts in a textile mill in Anqing, China, were recruited into the study during 1996–1998. The Human Subjects Committees at the Harvard School of Public Health and the China Medical Institutes approved all study procedures, and informed consent was obtained from each participant (Cho et al. 2002; Ronnenberg et al. 2000). Daily early morning urine samples were collected by the subjects during consecutive menstrual cycles. Paired sequential cycles were identified in which one of the pair was longer than the other. Of the 21 subjects enrolled, 9 subjects were excluded from the study because of noncompliance with the study protocol. Five subjects did not collect daily urine samples during the luteal-follicular phase transition (LFPT). Samples collected from the other 4 excluded subjects were too dilute to provide reliable information for follicular phase determination, as shown by low levels of creatinine in the sample (< 0.2 mg/mL). There was no association between the noncompliance of the subjects and their work shift schedules, and no other criteria were used to exclude subjects from the study.

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P. Lohstroh and J. Chen contributed equally to this paper.

The research described in this paper was funded by National Institutes of Health grants ES06198, ES05707, and P42 ES04699.

Received 9 July 2002; accepted 9 December 2002.